



Quantification of biomass and cell motion in human pluripotent stem cell colonies.

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Public Summary:

Somatic cell reprogramming to pluripotency requires an immediate increase in cell proliferation and reduction in cell size. It is unknown whether proliferation and biomass controls are similarly coordinated with early events during the differentiation of pluripotent stem cells (PSCs). This impasse exists because PSCs grow in tight clusters or colonies, precluding most quantifying approaches. Here, we investigate live cell interferometry as an approach to quantify the biomass and growth of HSF1 human PSC colonies before and during retinoic acid-induced differentiation. We also provide an approach for measuring the rate and coordination of intracolony mass redistribution in HSF1 clusters using live cell interferometry images. We show that HSF1 cells grow at a consistent, exponential rate regardless of colony size and display coordinated intracolony movement that ceases with the onset of differentiation. By contrast, growth and proliferation rates show a decrease of only approximately 15% decrease during early differentiation despite global changes in gene expression and previously reported changes in energy metabolism. Overall, these results suggest that cell biomass and proliferation are regulated independent of pluripotency during early differentiation, which is distinct from what occurs with successful reprogramming.

Scientific Abstract:

Somatic cell reprogramming to pluripotency requires an immediate increase in cell proliferation and reduction in cell size. It is unknown whether proliferation and biomass controls are similarly coordinated with early events during the differentiation of pluripotent stem cells (PSCs). This impasse exists because PSCs grow in tight clusters or colonies, precluding most quantifying approaches. Here, we investigate live cell interferometry as an approach to quantify the biomass and growth of HSF1 human PSC colonies before and during retinoic acid-induced differentiation. We also provide an approach for measuring the rate and coordination of intracolony mass redistribution in HSF1 clusters using live cell interferometry images. We show that HSF1 cells grow at a consistent, exponential rate regardless of colony size and display coordinated intracolony movement that ceases with the onset of differentiation. By contrast, growth and proliferation rates show a decrease of only approximately 15% decrease during early differentiation despite global changes in gene expression and previously reported changes in energy metabolism. Overall, these results suggest that cell biomass and proliferation are regulated independent of pluripotency during early differentiation, which is distinct from what occurs with successful reprogramming.

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